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(54) Title: BARRIER COATINGS FOR SURFACES

(57) Abstract

Articles having a surface intended for contact with an external biological environment, at least a portion of the surface comprising a stable coating capable of serving as an effective barrier to the passage of molecules between the surface and the environment.

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BARRIER COATINGS FOR SURFACES

TECHNICAL FIELD

In one aspect, the present invention relates to articles such as latex rubber gloves, and to methods aimed at reducing the incidence of problems attributable to the leaching of immunogenic proteins from such gloves to the skin of the wearer in the course of their use.

In a preferred embodiment, the invention relates to medical articles prepared from materials such as latex rubber, silicone rubber and woven and nonwoven fabrics, and to methods of reducing the adsorption or attraction of pathogenic molecules and particles onto such materials, the leaching of molecules from such materials or the passing of molecules or particles through such materials.

CROSS REFERENCE TO RELATED APPLICATIONS

This application is a continuation-in-part of U.S. Application Serial No. 07/816,771, filed January 2, 1992, entitled "Preparation of Polymeric Surfaces", which is a continuation of U.S. Application Serial No. 07/675,604, filed March 25, 1991, which is a divisional of U.S. Application Serial No. 07/447,802, (Pat. No. 5,002,582) filed December 8, 1989, which is a divisional of U.S. Application Serial No. 07/223,149, filed July 22, 1988, which is a continuation-in-part of U.S. Application Serial No. 07/138,226, filed December 24, 1987, which is a continuation-in-part of U.S. Application Serial No. 06/920,567, (Pat. No. 4,979,959) filed October 17, 1986, and of U.S. Application Serial No. 07/108,765, (Pat. No. 4,973,493) filed October 15, 1987, which is a continuation-in-part of U.S. Application Serial No. 06/428,074, (Pat. No. 4,722,906) filed September 29, 1982.

BACKGROUND OF THE INVENTION

A variety of materials are used for the preparation of articles such as medical devices. In the course of their use, however, it has become increasingly apparent that many of such materials may have undesirable properties. In particular, such properties often relate to the ability of such materials to either cause or promote allergic or other

pathogenic reactions with or within the body. Such reactions can be attributable, for instance, to either the adsorption of substances on or into the articles from their environment, or to the release of substances from the articles themselves.

For instance, skin sensitivities to materials such as latex rubber have been known for many years. It is estimated that 1% of the general population and 5-10% of health care professionals are sensitive to latex rubber, some to the point of developing anaphylactic responses. (See, for example, Tomazic, V.J., T.J. Withrow, B. Fisher and S.F. Dillard, "Latex-Associated Allergies and Anaphylactic Reactions", Clinical Immunology and Immunopathology 64: 89 (1992)). During the 1980's, the incidence of allergies to latex has appeared to increase significantly. This apparent increase may be the result of both improved diagnostic methods and increasing exposure to latex rubber and other materials in medical applications.

It has been shown that there exist both cell-mediated ("Type IV") and immunoglobulin E (IgE)-mediated ("Type I") hypersensitivities to latex rubber. Type IV hypersensitivity is thought to be caused primarily by a variety of accelerators, vulcanizers and antioxidants used in the manufacture of rubber products (See, for example, Von Hintzenstern, J., A. Heese, H.U. Koch, K.-P. Peters and O.P. Hornstein, "Frequency, Spectrum and Occupational Relevance of Type IV Allergies to Rubber Chemicals", Contact Dermatitis 24: 244 (1991)).

IgE-mediated hypersensitivity can range from urticaria to anaphylaxis, and can be life threatening. The allergens that cause this type of hypersensitivity appear to be provided by proteinaceous materials that are typically present in commercial latex. It is believed that such materials are able to leach out in the course of the use of the material, in a manner that allows them to contact the skin of the user.

It has been estimated that unprocessed raw latex contains approximately 2-3% protein, by weight (See Tomazic, V.J., et al. above). Some of the protein is removed during processing, but varying amounts will remain. The actual amount of protein remaining in the material will depend in large part on the process used for making the finished products. The allergens range in molecular weight from about 100,000 to 10,000 daltons (See, e.g., Chambeyron, C., J. Dry, F. Leynadier, C. Pecquet and Tran Xuan Thao, "Study of the Allergenic Fractions of Latex", Allergy 47: 92 (1992)).

Latex rubber is widely used in the medical industry and its use has increased

significantly in recent years. Some uses include the manufacture of surgeon's and exam gloves, urinary and other types of catheters, anesthesia ventilators, stoppers for vials, syringe plungers and dental polishers. With the rapid increase in HIV-infected patients, the use of latex rubber gloves has increased dramatically. This, in turn, has resulted in increased exposure to latex by both medical personnel and patients.

Adding to the problem with latex gloves is the use of powder for improving donning lubricity. The allergens appear to adsorb to the powder, which in turn can serve as a vehicle for further spreading the allergens into the air or to other sites of exposure such as door knobs and faucet handles.

Alternative materials can be used to prepare many of the medical products that are presently prepared using latex. Such other materials, however, are typically more expensive, and have less desirable elastic and functional properties than those of latex rubber. Although it is possible to find substitute materials for those who are most sensitive or at particular risk, it is not practical to entirely eliminate the use of latex rubber for all medical products.

There exist other situations in which the use of potentially allergenic or immunogenic materials in medical devices or articles can cause a problem. Silicone rubber, for instance, is widely used for implanted medical devices, including ventriculoperitoneal shunts, artificial joints, blood vessel grafts, angioplasty balloons, ocular lenses, heart valves, testicular prostheses and breast implants. Silicone implants, however, have been demonstrated to cause immune responses in some individuals over the course of long term exposure. It appears that either autoimmune responses to silicone-protein complexes or antibody induction against silicone polymers can result from silicone implants. The release of solubilized silicone from such implants could conceivably contribute to the problem.

Certain attempts have been made to address the drawbacks associated with the use of such materials. One approach to preventing exposure to latex allergens is to extensively wash or extract the allergens from the latex during the production of the latex articles. In another approach, a product identified as a "Biogel" glove, and available from Regent Hospital Products, Ltd. is claimed to have the "lowest anaphylactic rate of any surgical glove", by virtue of the use of a biocompatible hydrogel inner lining. See, e.g., "The Biogel Glove", Clinica Nov. 20th, page 22 (1991) and MedPRO Month Vol. III No. 3, page 44

(March 1993). See also, U.S. Pat. Nos. 3,813,695, 4,482,577, 4,499,154, 4,548,844, 4,575,476 and European Patent Application 0 455 323 A2.

It is clear that there exists in the industry a need to develop materials and processes that diminish the above-described drawbacks commonly associated with the use of articles such as medical articles. A further need exists for providing protective means to prevent pathogenic mediators from passing from or through the surfaces of materials that are themselves intended to provide protection against the spread of diseases. Such means should particularly be useful in a manner that does not detrimentally affect the desirable properties of the materials.

SUMMARY OF THE INVENTION

The present invention provides an article useful for contact with a biological environment, the article comprising a surface bearing a stable polymeric coating capable of serving as a "barrier" to the passage of pathogenic mediators between the surface and the biological environment. The barrier is capable of being stably applied to the surface in a manner that allows it to be retained in place over the course of the use of the article, yet does not detrimentally affect the desired properties of the article.

In another aspect, the invention provides a method of preparing such an article, comprising the step of providing at least a portion of the surface of the article with a stable coating capable of serving as an effective barrier to the passage of pathogenic mediators. The invention further provides an article bearing such a coating in apposition to a biological environment.

In a preferred embodiment the invention provides medical articles manufactured using materials such as latex rubber, silicone rubber, or woven or non-woven fabrics, the surface of such materials bearing a barrier coating of a type described herein. The barrier coating is capable of establishing a barrier to the passage of pathogenic mediators between the article and the body, for example, it substantially prevents the release of allergens from or through the article, and prevents the passage of immune cells from the host to the surface itself.

This application is a continuation-in-part of U.S. application Serial No. 07/816,771, the disclosure of which is incorporated herein by reference. The method of the invention described in applicant's earlier application involves activating latent reactive groups attached to polymer molecules to cause formation of covalent bonds between the

polymer and the substrate to provide a surface with the properties of the polymer.

Applicant has now found that polymer molecules having latent reactive groups can be stably immobilized onto a surface to achieve a physical barrier that can exclude certain molecules, such as macromolecules, from penetrating the polymer layer. In a preferred embodiment, the invention relates to medical devices and other articles having surfaces that are intended to contact biological substances, including tissues and fluids of the body. In another aspect, the invention relates to materials useful for manufacturing such articles and surfaces. The invention further relates to methods and means useful for reducing the possibility of deleterious effects of such materials when placed in contact with the body.

In a particularly preferred embodiment applicant has discovered that such barrier coatings are effective in preventing macromolecules such as allergens from attaching to or leaching from medical articles prepared from materials such as latex rubber. It appears that allergen leaching from latex rubber can be reduced by as much as 90% or more as compared with uncoated latex.

The barrier coatings of the present invention, therefore, provide a particularly optimal combination of effectiveness, ease of application, cost and versatility, particularly for use as coatings for medical articles prepared from latex rubber, silicone rubber, and woven and nonwoven fabrics.

DESCRIPTION OF THE PREFERRED EMBODIMENT

As used herein the following terms and words shall have the meanings ascribed to them:

"polymeric coating compound" shall refer to a polymer having latent reactive groups and capable of being immobilized on or to a surface, e.g., by activating the latent reactive groups to form a tightly crosslinked layer, in order to provide the surface with a physical barrier to the passage of pathogenic mediators;

the terms "pathogenic mediator" and "mediator of pathologic response" shall refer to molecules such as macromolecules, including antigens and antibodies, and particles such as viral particles and cells, having the potential to elicit a pathologic, e.g., immunologic, response in a living host, such mediators being capable of movement between an article and a biological environment provided by the host;

"article" shall refer to an object fabricated, at least in part, from a material as

described herein, the article having a surface intended for use in physical (e.g., fluid) contact with a biological substance, and preferably with a body tissue or fluid;

"material" shall refer to the chemical makeup of the surface of an article, for instance, a latex rubber or silicone rubber;

"surface" shall refer to any interface between an article and a biological environment having the potential to allow the passage of pathogenic mediators between the article and the environment;

"coating", when used as the noun, shall refer to an immobilized polymeric layer on a surface, the coating being useful as a barrier between a surface and its environment;

"barrier" shall refer to the ability of a coating to substantially prevent the passage of pathogenic mediators between a surface and its environment;

A preferred polymeric coating compound of the present invention includes photoactivatable polyacrylamide having sufficiently low molecular weight and a sufficiently high level of photogroups to achieve a level of crosslinking sufficient to provide an effective barrier when coated onto a surface and photoactivated. Preferably the polymer is not only coupled to the surface via the photogroups but also becomes crosslinked to form a membrane-like coating.

The polymers of the invention are preferably chosen so as to form either a tightly crosslinked layer or a densely packed layer on the surface, in order to prevent soluble macromolecules or particulates, such as pathogenic viruses or bacteria, from penetrating the barrier. In one embodiment, the polymer is a photopolymer of relatively low molecular weight and relatively high level of photoactivatable groups such that the polymer can photochemically couple both to the surface and to the polymer to form a tightly crosslinked excluding layer. In another embodiment, two photopolymers are used, one which contains reactive functional groups capable of reacting thermochemically with appropriate functional groups on the other.

While not intending to be bound by theory, it appears that the barrier effect is based at least in part on principles of size exclusion. In addition, the barrier might simply serve to lessen the degree to which a permeable surface is constantly flushed or bathed with fluids from a biological environment, thereby lessening the rate at which materials might be adsorbed or leached from the surface.

Preferred polymers used for preparing barrier coatings include photoactivatable

derivatives of polyacrylamide, polyethylene glycol, polyvinylpyrrolidone, dextran or many other relatively hydrophilic polymers. The polymers can also include charged groups, such as carboxylic acid, sulfonic acid, quaternary ammonium or primary, secondary or tertiary amines. Examples of charged monomers that can be incorporated into the polymers used for barrier coatings include 2-acrylamido-2-methylpropanesulfonic acid and methacrylamidopropyltrimethylammonium chloride.

The mediators to be excluded by the barrier coating can be proteins or other macromolecules, either within the article itself (e.g., latex rubber proteins) or present in solutions or substances (e.g., bodily fluids or tissues) contacting the article. Examples of the latter include blood proteins, other blood or tissue molecules or macromolecules in other solutions that contact the article. Other macromolecules to be excluded by the barrier coatings of this invention include polymers that would be released from the solid in the absence of the coating, either by breakdown of the solid polymer or by leaching of oligomers from within the bulk polymer.

Other types of biological macromolecules that might be desirable to exclude by the barrier coatings of this invention include lipids, nucleic acids, carbohydrates or any types of conjugated biological macromolecules, such as lipoproteins, glycolipids or glycoproteins. Particles that are desirable to exclude by the barrier coatings of this invention include viruses, bacteria or fungi in solutions contacting the solid to be coated. Such particles can also can include insoluble fragments of material released from the solid to be coated.

In a particularly preferred embodiment the barrier coating consists of photopolyacrylamide containing benzophenone groups on the polymer (between 2 and 4 mole percent) and having a molecular weight of between 10,000 and 50,000 daltons. Typically the polymer is first applied to the surface, after which the photoactivatable groups are activated by illumination to form a tightly crosslinked coating on the surface.

The method of the present invention is useful with articles prepared from a variety of materials, including latex rubber, silicone elastomers or polypropylene nonwoven fabrics. In a preferred embodiment the method is used to coat articles prepared using latex rubber or silicone rubber materials. The term "latex rubber", as used herein, refers to natural rubber and its derivatives. Commercial grade natural rubber typically includes about 93-95 weight % cis-1,4-isoprene. The nonrubber portion typically contains about

2-3 weight % protein, together with other materials. See generally, "Rubber, Natural", pages 1013-1017, in Concise Encyclopedia of Polymer Science and Engineering, J. Kroschwitz, ed., Wiley & Sons, 1990, the disclosure of which is incorporated herein by reference.

The term "silicone rubber", as used herein, refers to rubbers such as "RTV" (room temperature vulcanized) and heat-cured rubbers, as described in "Silicones", pages 1048-1059, in Concise Encyclopedia of Polymer Science and Engineering, J. Kroschwitz, ed., Wiley & Sons, 1990, the disclosure of which is incorporated herein by reference.

The term "nonwoven fabrics", as used herein, refers to synthetic fabrics such as melt blown or spun bond polypropylene. See, for example, "Nonwoven Fabrics", pages 655-660, in Concise Encyclopedia of Polymer Science and Engineering, J. Kroschwitz, ed., Wiley & Sons, 1990, the disclosure of which is incorporated herein by reference. See also Leonas, K.K., "Evaluation of Five Nonwoven Surgical Gowns as Barriers to Liquid Strikethrough and Bacterial Transmission", INDA Journal 5:22 (1993) and Dusaj, S. "Making Composite Barrier Fabrics for Healthcare Workers", Technical Textiles International, March 1993, p. 20.

The method of the present invention is able to provide a coating that provides a barrier to immunological reaction, e.g., substantially reduces the leaching of allergens from a material, the adsorption of antibodies or other biomolecules to a material or passage of molecules or particles through the material. The coatings are able to function without "detrimental effect" on the properties for which the material is intended to be used, i.e., without affecting properties of the material to a point where it is no longer suitable for its intended purpose.

Articles made from such materials include medical articles used externally to the body, such as gloves and gowns, and medical articles to be implanted in or on the body. Examples of such devices include gloves, catheters, grafts, implants, balloons, valves, prostheses, and the like. In particular, such articles prepared using latex include gloves such as surgeon's and exam gloves, condoms, catheters such as urinary catheters, anesthesia ventilators, stoppers for vials that are to contain biological substances or substances for biological use, syringe plungers and dental polishers. Silicone rubber, for instance, is widely used for implanted medical devices, including ventriculoperitoneal shunts, artificial joints, blood vessel grafts, angioplasty balloons, ocular lenses, heart

valves, testicular prostheses and breast implants. Barrier coatings can also be used for preventing pathogenic viruses or bacteria in body fluids from passing through medical fabrics, such as surgical drapes and surgeon's gowns, typically made from nonwoven polypropylene.

The coating compounds employed in the present invention are polymeric in nature, that is, they have repeating units and a molecular weight distribution. Most preferably, the coating compounds are derived from or formed as synthetic polymers. The polymers of the invention include oligomers, homopolymers and copolymers resulting from addition or condensation polymerization, and natural polymers including nucleic acids, oligosaccharides, linear polysaccharides such as amylose, dextran, chitosan, heparin and hyaluronic acid, and branched polysaccharides such as amylopectin, glycogen and hemicelluloses. The polymers may include several distinct polymer types, as may be prepared by terminal or side chain grafting. The polymers of the invention may include cellulose-based products such as hydroxyethyl cellulose, hydroxypropyl cellulose, carboxymethyl cellulose, nitrocellulose, cellulose acetate and cellulose butyrate, acrylics such as those polymerized from hydroxyethyl acrylate, hydroxyethyl methacrylate, glyceryl acrylate, glyceryl methacrylate, acrylic acid, methacrylic acid, acrylamide and methacrylamide, vinyls such as polyvinyl pyrrolidone and polyvinyl alcohol, nylons such as polycaprolactam, polylauryl lactam, polyhexamethylene adipamide and polyhexamethylene dodecanediamide, polyurethanes and polylactic acids.

Of particular importance are the vinyl polymers such as polyvinyl pyrrolidone and polyacrylamide and the polyethers such as polyethylene glycol. For brevity, the invention is described below primarily with respect to the use of single coating compounds that are homopolyfunctional (that is, that bear two or more identical latent reactive groups (and such is preferred)). However, one may employ a mixture of polymeric coating compounds, if desired, and the coating compounds themselves may be heteropolyfunctional (that is, they may contain two or more different latent reactive groups) and they may have different properties which they confer upon the matrix.

The polymeric coating compounds employed in the invention desirably are soluble or at least dispersible in a solvent (to form, for example, a colloidal suspension), and preferably are soluble in water to at least the extent of 1 gram/liter at 23°C. A "latent reactive group", as used herein, refers to a chemical group that responds to an applied

external energy source in order to undergo active specie generation, resulting in covalent bonding to an adjacent chemical structure (e.g., an abstractable hydrogen). Preferred groups are sufficiently stable to be stored under conditions in which they retain such properties. See, e.g., U.S. Patent No. 5,002,582, the disclosure of which is incorporated herein by reference. Latent reactive groups can be chosen that are responsive to various portions of the electromagnetic spectrum, with those responsive to ultraviolet and visible portions of the spectrum (referred to herein as "photoreactive") being particularly preferred.

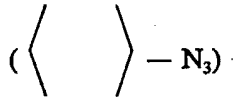
Latent reactive groups respond to specific applied external stimuli to undergo active specie generation with resultant covalent bonding to an adjacent chemical structure, e.g., as provided by the same or a different molecule. Latent reactive groups are those groups of atoms in a molecule that retain their covalent bonds unchanged under conditions of storage but that, upon activation by an external energy source, form covalent bonds with other molecules.

The latent reactive groups generate active species such as free radicals and particularly nitrenes, carbenes, and excited states of ketones upon absorption of external electric, electromagnetic or kinetic (thermal) energy. Latent reactive groups may be chosen to be responsive to various portions of the electromagnetic spectrum, and latent reactive groups that are responsive to e.g., ultraviolet and visible portions of the spectrum are preferred and are referred to herein occasionally as "photochemical" groups.

Photoreactive aryl ketones such as acetophenone and benzophenone, or their derivatives, are preferred, since these functional groups, typically, are readily capable of undergoing the activation/inactivation/reactivation cycle described herein. Benzophenone is a particularly preferred photoreactive group, since it is capable of photochemical excitation with the initial formation of an excited singlet state that undergoes intersystem crossing to the triplet state. The excited triplet state can insert into carbon-hydrogen bonds by abstraction of a hydrogen atom (from a support surface, for example), thus creating a radical pair. Subsequent collapse of the radical pair leads to formation of a new carbon-carbon bond. If a reactive bond (e.g., carbon-hydrogen) is not available for bonding, the ultraviolet light-induced excitation of the benzophenone group is reversible and the molecule returns to ground state energy level upon removal of the energy source. Hence, photoreactive aryl

ketones are particularly preferred.

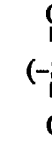
The azides constitute a preferred class of latent reactive groups and include arylazides



such as phenyl azide and particularly 4-fluoro-3-nitrophenyl azide, acyl azides

such as benzoyl azide and p-methylbenzoyl azide, azido formates

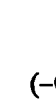
such as ethyl azidoformate, phenyl azidoformate, sulfonyl azides



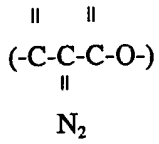
such as benzenesulfonyl azide, and phosphoryl azides

such as diphenyl phosphoryl azide and diethyl phosphoryl azide. Diazo compounds constitute another class of latent reactive groups and include diazoalkanes ($-CHN_2$) such as diazomethane and diphenyldiazomethane, diazoketones

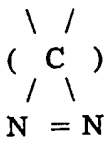
such as diazoacetophenone and 1-trifluoromethyl-1-diazo-2-pentanone, diazoacetates



such as t-butyl diazoacetate and phenyl diasoacetate, and beta-keto-alpha-diazoacetates



such as t-butyl alpha diazoacetoacetate. Other latent reactive groups include the aliphatic azo compounds such as azobiscyanovaleric acid, the diazirines



such as 3-trifluoromethyl-3-phenyldiazirine, and the ketenes (-CH=C=O) such as ketene and diphenylketene. Photoactivatable aryl ketones such as benzophenone and acetophenone are of particular importance inasmuch as these groups are subject to multiple reactivation in water and hence provide increased coating efficiency. Peroxy compounds are contemplated as another class of latent reactive groups and include dialkyl peroxides such as di-t-butyl peroxide and dicyclohexyl peroxide and diacyl peroxides such as dibenzoyl peroxide and diacetyl peroxide and peroxyesters such as ethyl peroxybenzoate.

Upon activation of the latent reactive groups, the coating compounds are covalently bound to each other and/or to the surface of the article by covalent bonds through residues of the latent reactive groups. Exemplary latent reactive groups, and their residues upon activation, are as follows:

Latent Reactive Group	Residue Functionality	
aryl azides	amine	R-NH-R'
acyl azides	amide	R-C-NH-R'
azidoformates	carbamate	R-O-C-NH-R'
sulfonyl azides	sulfonamide	R-S-NH-R'
phosphoryl azides	phosphoramide	$(RO)_2$P-NH-R'

diazoalkanes	new C-C bond
diazoketones	new CC bond & ketone
diazoacetates	new C-C bond & ester
beta-keto-alpha-diazoacetates	new C-C bond & beta-ketoester
aliphatic azo	new C-C bond
diazirines	new C-C bond
ketenes	new C-C bond
photoactivated ketones	new C-C bond & alcohol
dialkyl peroxides	ethers
diacyl peroxides	esters & new CC bonds
peroxyesters	ethers, esters, and new C-C bonds

The coating compounds of the invention desirably have an average of at least two and preferably three or more latent reactive groups per molecule. Three-dimensional molecular networks may be formed through the use of polymeric coating compound molecules each having two or more latent reactive groups. In general, the density of covalent bonds resulting from activation of the reactive groups and hence the "tightness" of the three-dimensional molecular network that is formed will be increased by decreasing the distance between latent reactive groups that are employed in the coating compound.

Depending upon the method of fabrication of the polymeric coating compound, that compound may contain varying numbers of latent reactive groups. A bifunctional polymeric coating compound may have one latent reactive group at each of its two ends. For example, 4-bromomethylbenzophenone (derived from the free radical bromination of 4-methylbenzophenone) may be reacted with polyethylene glycol to form a bifunctional coating compound having $-(CH_2-CH_2-0)-$ repeating units and terminating in benzophenone

latent reactive groups.

Polymeric coating compounds used in the invention may have latent reactive groups incorporated at random positions along the polymer backbone. It may in some instances be desirable to provide polymers with more predictable sites for attachment of latent reactive groups. Polymeric coating compounds desirably, but not necessarily, have latent reactive groups at their ends or at random locations along their backbones (spaced from their ends) or both. By "backbone" as used herein in connection with polymer molecules, reference is made to the chain of atoms that is characteristic of the polymer and that results from the polymerization reaction. For example, polyethylene glycol polymers are characterized by a "backbone" of repeating -(-CH_2-CH_2-O-)- groups, whereas polyacrylamide and polyvinyl pyrrolidone have backbones characterized by carbon-carbon bonds, alternating carbon atoms in the backbone having pendent amide or pyrrolidone groups, respectively.

A polymer that includes at least one latent reactive group along its backbone spaced from its ends can be prepared by copolymerizing the basic monomer or monomers for the polymer with a monomer to which can be readily attached a latent reactive group such as a photoreactive group. For example, a photoreactive polyacrylamide polymer can be obtained by copolymerizing acrylamide with a small quantity of N-(3-aminopropyl)methacrylamide to provide random amine-functional groups along the polymer backbone, and then reacting the polymer with an amine-reactive photoreactive reagent such as benzoylbenzoylchloride.

Coating compounds may be derived from naturally occurring polymers such as hyaluronic acid by known methods such as those taught in U.S. Patent 5,002,582, the teachings of which are incorporated herein by reference. The tightness of the three-

dimensional network that is formed will depend upon the density of covalent bonds formed from the latent reactive groups carried by the coating compound and the molecular weight and the ability of the polymeric coating compound to pack tightly on the surface. The method of the invention finds particular utility, however, in the formation of a coating upon a surface, desirably a solid surface, to which the film becomes covalently bonded by latent reactive groups of the coating compound. In this embodiment, the surface itself becomes chemically involved in the formation of the three-dimensional matrix. Such surfaces preferably have abstractable hydrogen atoms and participate readily in the formation of covalent bonds upon activation of the latent reactive groups.

In the preferred process of the invention, the coating compound is applied to a surface, and the latent reactive groups of the coating compounds are simultaneously reacted to form covalent bonds between the coating compound and the surface and between different molecules of the coating compound, to form a three dimensional molecular network.

To facilitate the coating process, the polymeric coating compound is applied to a surface from a solvent medium, preferably from solution and most preferably from aqueous solution. Preferably, the coating compound is in solution and applied as a wet film to the surface, following which the latent reactive groups are activated, by light, in the case of photoreactive groups. Solvent may be partially or totally removed from the wet film before activation of the latent reactive groups. Alternatively, the latent reactive groups may be reacted in the presence of the solvent.

The invention may be more easily understood by reference to the following illustrative, non-limiting examples:

EXAMPLE 1

Synthesis of Photoactivatable Polyacrylamide

One gram of acrylamide (14.1 mmole) was dissolved in 10 ml of tetrahydrofuran. To this solution was added 175 mg of benzoylbenzoyl-aminopropylmethacrylamide (0.5 mmole) (previously synthesized by reacting benzoylbenzoyl chloride with 3-aminopropylmethacrylamide) and 50 mg of azobisisobutyronitrile. The solution was sparged with argon, sealed, then put at 55°C overnight to polymerize. The resulting polymer was collected by filtration, then dissolved in deionized water, dialyzed against deionized water and lyophilized.

EXAMPLE 2

Coating of Latex Rubber to Prevent Allergen Leaching

Latex balloons useful as covers for rectal probes used in imaging procedures were coated with the photopolyacrylamide of Example 1. The balloons were first thoroughly cleaned with an isopropyl alcohol (IPA) wipe. Following IPA the balloons were dipped into a solution of 15 mg/ml photopolyacrylamide in 20% isopropanol. The balloons were removed from the solution, and while still wet, were centered in a Dymax brand light chamber between two lamps set 20 inches apart, where they were then illuminated until dry (2 minutes). The coating and illumination procedure was repeated to provide a total of two coats. The balloons were thoroughly washed with water, dried and stored until tested. The balloons were tested for latex leaching by extracting proteins from the surface and measuring allergens with an immunoblot assay using a pool of serum from allergic patients. A preliminary comparison of uncoated vs. coated balloons showed greater than 90% reduction in allergens extracted. The balloons appeared to retain their desirable physical properties in that they remained pliant and extensible, as well as

visually indistinguishable from uncoated balloons.

EXAMPLE 3

Coating of Silicone Rubber to Prevent Blood Plasma Proteins from Binding to the Silicone

Pieces of Silastic ™ medical grade tubing were rinsed with hexane to clean the surface, soaked in IPA for one minute, then illuminated by placing the pieces of tubing 15 cm from a Dymax brand lamp for four minutes. The silicone pieces were then dipped into a solution of photo-poly(vinylpyrrolidone/acrylamidomethylpropane sulfonic acid) at 10 mg/ml in water. The pieces were then illuminated for two minutes using the same light conditions described above. The pieces were then dipped into a solution of photo-polyacrylamide at 10 mg/ml and again illuminated as above. Finally, the silicone was thoroughly washed with water. The silicone rubber coated in this manner reduced the adsorption of radiolabeled human gamma globulin by approximately 60% as compared to untreated silicone.

EXAMPLE 4

Coating of Melt Blown Polypropylene to Prevent Blood Borne Viruses and Bacteria Through the Fabric

To a melt blown polypropylene fabric is applied a solution of the polymer of Example 1 in aqueous solution at 15 mg/ml. The solution is applied to the surface of the fabric and spread across the surface by rolling a glass rod across the fabric with enough pressure to compress the fabric under the rod. The solution is then dried on the fabric and illuminated with uv light. The coating formed will prevent passage of viruses, blood cells, bacteria or other microorganisms through the fabric.

CLAIMS

What is claimed is:

1. An article useful for contact with a biological environment, the article comprising a surface bearing a stable polymeric coating capable of serving as a barrier to the passage of pathogenic mediators between the surface and the biological environment.

2. An article according to claim 1 wherein the article is a medical article fabricated from a material selected from the group consisting of latex rubber, silicone rubber, and non-woven fabrics.

3. An article according to claim 2 wherein the material is latex rubber.

4. An article according to claim 2 wherein the material is silicone rubber.

5. An article according to claim 2 wherein the material is a non-woven fabric.

6. An article according to claim 1 wherein the pathogenic mediators are selected from the group consisting of macromolecules, viral particles and whole cells.

7. An article according to claim 6 wherein the mediators are macromolecules selected from the group consisting of antigens, antibodies, and blood proteins.

8. An article according to claim 1 wherein the polymers of the coating are covalently bound to each other and to the surface to form a crosslinked matrix.

9. An article according to claim 1 wherein the article is selected from the group consisting of medical articles used externally to the body and medical articles to be implanted in or on the body.

10. An article according to claim 9 wherein the article is a latex glove.

11. A combination comprising an article in apposition to a biological environment, the article comprising a surface bearing a stable polymeric coating capable of serving as a

barrier to the passage of pathogenic mediators between the surface and the biological environment.

12. A method of preparing an article having a surface intended for contact with an external environment, comprising the step of providing at least a portion of the surface with a stable polymeric coating capable of serving as a barrier to the passage of pathogenic mediators between the surface and the biological environment.

INTERNATIONAL SEARCH REPORT

International Application No
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A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61L27/00 A61L31/00 A61L29/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO,A,81 00345 (AMERICAN HOSPITAL SUPPLY CORP.) 19 February 1981 see claims; examples 1-2 ---	1-12
X	EP,A,0 397 130 (KANEGAFUCHI KAGAKU KOGYO KK) 14 November 1990 see page 6, line 45 - line 52; claims ---	1-9
X	WO,A,89 04647 (STILLMAN S.) 1 June 1989 see claims; examples ---	1-7
X	EP,A,0 106 004 (INTERNATIONAL SILICONE CORP.) 25 April 1984 see the whole document ---	1-5

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
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Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+ 31-70) 340-2040, Tx. 31 651 epo nl, Fax (+ 31-70) 340-3016	ESPINOSA, M

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A	EP,A,0 113 526 (LRC PRODUCTS LIMITED.) 18 July 1984 see claims; example ---	1-12
A	WO,A,88 02623 (BIO-METRIC SYSTEMS, INC.) 21 April 1988 cited in the application see claims & US,A,4 979 959 -----	1-12

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